

Remarks

Claims 11-12 and 18-20 are pending. Claims 18 and 19 are withdrawn due to a previous Restriction Requirement and election. By way of this Amendment, claims 11 and 20 have been amended, and claims 26-28 (directed to withdrawn subject matter) have been newly added. No new matter has been added.

Request to Change Elected Group to Group III (Claims 26-28)

This Response is filed in conjunction with a Request for Continued Examination (RCE). Upon reopening of prosecution, Applicants respectfully request to change the elected group from Group I (currently claims 11, 12, and 20) to Group III (newly presented claims 26-28) as those groups were identified in the Restriction Requirement mailed July 23, 2008. Newly presented claims 26-28 correspond to claim 15 of the originally-filed specification and are supported by page 3, ll.6-11, page 4, ll.6-18, and page 8, ll. 32-33 of the originally-filed specification.

The novelty and differences from the cited art are particularly highlighted by the claims of Group III. However, the remarks below apply equally to the previously elected claims and should be considered even if the Office declines to change the elected group.

Claim Rejection Under 35 USC 112, Second Paragraph

Claim 20 are rejected under 35 USC 112, second paragraph, as indefinite. Claim 20 has been amended in order to correct the indefiniteness.

Claim Rejections Under 35 USC 103

Claims 11, 12, and 20 are rejected under 35 USC 103(a) over Box et al. WO 03/024439 in view of Keller et al. 6,645,466. The Office accurately characterizes Box as disclosing the claimed active ingredient 4-((1*R*)-2-[(6-{2-[(2,6-dichlorobenzyl)oxy]ethoxy}hexyl)amino]-1-hydroxyethyl)-2-(hydroxymethyl)phenol and its optional use in combination with lactose. The Office also accurately characterizes Keller as disclosing the concept of combining an active agent (in general) with magnesium stearate for the

purpose of improving moisture resistance. The Office alleges that one of ordinary skill in the art would have been motivated to use the specific compound and formulation of Box with the magnesium stearate of Keller.

When combining references, we are guided in part by KSR, which instructs "The mere fact that references can be combined or modified does not render the resultant combination obvious unless **>the results would have been predictable to one of ordinary skill in the art." *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, 82 USPQ2d 1385, 1396 (2007) from MPEP 2143.01(III).

With regard to the demonstrated effect of reducing chemical degradation, Applicants have discovered that chemical degradation of the recited active ingredient, when in the presence of lactose, is inhibited by the addition of magnesium stearate. Inhibition of chemical degradation is not discussed in Box or Keller.

The inhibition of chemical degradation results in lower amounts of impurities over time at given temperatures and relative humidities. Reduction of impurities is, of course, of interest in the pharmaceutical area. As previously stated, neither of the cited references teaches or suggests the inhibition of chemical degradation of an active such as 4-((1*R*)-2-[(6-{2-[(2,6-dichlorobenzyl)oxy]ethoxy}hexyl)amino]-1-hydroxyethyl)-2-(hydroxymethyl)phenol. There is no indication that such degradation would be expected. On that basis, the references fail to disclose or suggest the invention, whether alone or combined.

With regard to moisture resistance, it is acknowledged by the Office that Keller fails to teach the use of magnesium stearate with the particular active recited in the claims. Applicants submit that, without contemplating the specific active, excipients, and manner in which the active was to be delivered, it would be impossible to know if addition of magnesium stearate would be appropriate as an additive. Indeed, the FDA and other regulatory agencies often specify that there be no extraneous components of a drug formulation. So, if the recited active and formulation were in no need of improved moisture resistance, or if the additive failed to provide improved

moisture resistance to this particular formulation, then the additive of Keller could actually be detrimental to the formulation, at least from a regulatory sense.

Review of the record with regard to the specific recited active ingredient shows 1) no teaching of a need for improved moisture resistance, 2) no showing that the active would benefit by addition of magnesium stearate, and 3) no discussion or showing that the formulation would not be harmed by addition of un-needed magnesium stearate.

In summary, Applicants were the first to discover and claim a formulation and/or method of inhibiting chemical degradation of the recited active ingredient with lactose. The cited references suggest that the moisture resistance of some active ingredients benefit from the addition of magnesium stearate, but the teachings fall far short of providing predictability for specific active ingredients such as the one recited in the pending claims.

As such, the results of the proposed combination may not be deemed to be predictable and, therefore, the rejection under 35 USC 103 should be withdrawn.

Conclusion

Applicants assert that the instant Amendment places the application in a condition for allowance, and such allowance is respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge any fees or credit any overpayment, particularly including any fees required under 37 CFR Sect 1.16 or 1.17, and any necessary

extension of time fees, to deposit Account No. 07-1392. The Examiner is invited to contact the undersigned at (919) 483-8160, to discuss this case, if desired.

Respectfully submitted,



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